Health effects of passive smoking · 1

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Parental smoking and lower respiratory illness in infancy and early childhood

David P Strachan, Derek G Cook

Abstract

Background **– A systematic quantitative review was conducted of evidence relating parental smoking to acute lower respiratory illness in the first three years of life.**

Methods **– Fifty relevant publications were identified after consideration of 692 articles selected by electronic search of the Embase and Medline databases using keywords relevant to passive smoking in children. The search, completed in April 1997, identified 24 studies ascertaining illnesses in a community setting, including five surveys of schoolchildren with retrospective ascertainment of early chest illness, and 17 studies of admissions to hospital for lower respiratory illness in early life. Thirty eight studies were included in a quantitative overview using random effects modelling to derive pooled odds ratios.**

Results **– The results of community and hospital studies are broadly consistent, with only one publication reporting a reduced risk among children of smokers. The pooled odds ratios were 1.57 (95% CI 1.42 to 1.74) for smoking by either parent and 1.72 (95% CI 1.55 to 1.91) for maternal smoking. There is a significantly increased risk of early chest illness associated with smoking by other household members in families where the mother does not smoke (1.29, 95% CI 1.16 to 1.44). The associations with parental smoking are robust to adjustment for confounding factors, and show evidence of a dose-response relationship in most studies in which this has been investigated.**

Conclusions **– The relationship between parental smoking and acute lower respiratory illness in infancy is very likely to be causal. Although it is impossible to distinguish the independent contributions of prenatal and postnatal maternal smoking, the increased risk associated with smoking by other household members suggests that exposure to environmental tobacco smoke after birth is a cause of acute chest illness in young children.**

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Two articles published in the *Lancet* in 1974[1 2] alerted readers to a possible link between parental smoking and the risk of lower respiratory illness in infancy. Although adverse effects from exposure of children to environmental tobacco smoke had been suggested previously,[3 4] the association with acute chest illness was of immediate and continuing interest because of the suspected long term consequences of early episodes for lung growth, chronic respiratory morbidity in childhood, and adult chronic obstructive lung disease.[5]

During the last two decades many epidemiological studies have reported upon the association of parental smoking and respiratory diseases throughout childhood. In this, the first of a series of systematic and quantitative reviews of health effects of passive smoking, we summarise the evidence relating specifically to acute lower respiratory illnesses in the first two or three years of life. Studies of asthma incidence, prognosis, and severity will be reviewed separately. Although there is some overlap with the studies of early wheezing illness included in this paper, the latter display certain characteristics which are distinct from asthmatic episodes of later onset. The problems of applying precise diagnostic labels to many infants with lower respiratory illness further justifies the inclusion of early wheezing illnesses in this review.

Methods

Published papers, letters, and review articles relating to passive smoke exposure in children were selected by an electronic search of the Embase and Medline databases. The Medline search strategies used were:

(1) To identify all passive smoking references:
   (a) MESH heading "*tobacco smoke pollution*";
   (b) {*passive* **or** *second-hand* **or** *second hand* **or** *involuntary* **or** *parent$* **or** *maternal* **or** *mother$* **or** *paternal* **or** *father$* **or** *household$*} **and** {*smok$* **or** *tobacco$* **or** *cigarette$*} where $ = wild card;
   (c) combine (a) **or** (b).

(2) To restrict to children:
(a) restrict (c) above to all relevant age groups;
(b) search (c) above for *paediatric$* **or** *pediatric$* **or** *infan$* **or** *child$* **or** *adolescen$*;
(c) combine (a) **or** (b).

The Embase strategy used was based on text word searches of titles, keywords, and abstracts for items listed in 1(b) **and** 2(b) above.

This search, completed in April 1997, yielded 3625 references of which 1593 contained keywords relevant to respiratory or allergic disease. These 1593 abstracts were reviewed and 692 were identified as of possible relevance to the assessment of respiratory health effects; 472 (68%) of these had been published during 1990–96, the remainder during 1972–89.

Among 75 publications which were considered in detail as of possible relevance to illnesses in infancy, 50 were included in this review, and 38 studies were included in quantitative meta-analyses: 10 case-control studies, 21 longitudinal studies, two controlled trials, and five cross sectional surveys of children of school age. The latter were included because they related parental smoking to a retrospective history of chest illness before two years of age (obtained by the American Thoracic Society children's questionnaire[6]). No additional references were identified by citations in the above papers or previous overviews.

Wherever possible, information was extracted from each study relating to the odds ratio for chest illness among children with and without smokers in the family, and separately for children exposed and unexposed to maternal smoking, whether during pregnancy or postnatally. We also addressed specifically the effect of smoking by other household members (usually the father) for children whose mother did not smoke. Not all these indices could be derived from each study. The most widely derived measures of effect related to either parent smoking (compared with neither) and the effect of mother smoking (compared with father only or neither parent smoking). Few studies distinguished in any detail between prenatal and postnatal maternal smoking, but those which did are discussed below.

The odds ratio was chosen as a measure of association which can be derived from all types of study (case-control, cross sectional and longitudinal).[7] In general, odds ratios and their 95% confidence intervals were calculated from data in published tabulations using the actual numbers of subjects or numbers derived approximately from percentages of published column or row totals. This approach allowed flexibility in combining categories of household smoke exposure for comparability across studies. Where the numbers of subjects were not shown, the published odds ratio and its 95% confidence interval were used. A few papers quoted an incidence rate ratio rather than an odds ratio, and these are identified in the summary tabulations. Information was also sought on the extent to which the effects of parental smoking were altered by adjustment for potential confounding variables, and whether there was evidence of a dose-response relationship – for instance, to the amount smoked by either parent. Only one paper from each study (usually the most recently published) was included in quantitative meta-analyses. However, in some studies information from other papers contributed to the assessment of confounding or dose-response relationship.

Where quantitative meta-analysis was considered appropriate, odds ratios were tested for heterogeneity using the technique of Breslow and Day.[8] The heterogeneity tests were often statistically significant, implying that a simple "fixed effect" pooling of the logarithms of the odds ratios (using weights inversely proportional to their variances[7]) may be inappropriate. Odds ratios were therefore pooled using a "random effects" model which makes allowances for heterogeneity of effect between studies. In practice, this approach produces estimates similar to those of standard methods but allows regression models to be fitted, if desired, in order to explain heterogeneity between studies.[9]

The random effects model was implemented by using iteratively reweighted least squares regression, adapting a method previously developed for geographical mortality studies.[10] This approach has the practical advantage that only the log odds ratios and their standard errors are required, and not the raw data from each individual study. The computing algorithm used for this purpose is shown in the Appendix.

The log odds ratios were used as dependent variables and their standard errors were used to estimate the component of variance between studies attributable to sampling variation. Any non-sampling variation, representing heterogeneity of passive smoking effects between studies, was assumed to be normally distributed with a mean of zero. 95% confidence intervals for the pooled odds ratio were calculated by assuming that the estimated log odds ratio divided by its standard error follows a t distribution on $(n-2)$ degrees of freedom where n is the number of studies pooled. In practice, this will produce confidence intervals which are too wide when n is small and there is little heterogeneity. For this reason, we do not present results from random effects models where fewer than five studies are pooled.

Results

COMMUNITY STUDIES OF LOWER RESPIRATORY ILLNESS

Twenty one studies[11–31] were identified in which lower respiratory illnesses had been ascertained in a community or ambulatory clinic setting and related to parental smoking (table 1). These comprised 14 longitudinal studies, two controlled trials, two case-control studies, and three retrospective prevalence surveys. In seven studies[12–14 19 20 22 23] all lower respiratory diagnoses were combined; four[11 15 17 21] contributed information on bronchitis and pneumonia, and two[16 18] concentrated on illnesses diagnosed as bronchiolitis. Ten studies[15 17 24–31] focused

Table 1 Design, sample size and recruitment criteria for studies included in meta-analyses

Reference	Year	Country	Age	Design	Outcome	Sample size	Case definition	Source of controls or cohort
Community studies: lower respiratory illnesses								
11	76	UK	<1 y	Cohort	Br/Pn	2074	Br/Pn (reported)	Population-based birth cohort
12	84	USA (TX)	<1 y	Panel	LRI	131	LRI (reported)	Virological surveillance panel
13	85	USA (DC)	<1 y	Cohort	LRI	1144	LRI consultation	Paediatric practice
14	85	USA[a]	<2 y	Survey	LRI	8528	PD RI before 2 years	Population survey: age 6–9 years
15	85	N Zealand	<2 y	Cohort	Br/Pn	1144	Br/Pn consultation	Population-based birth cohort
16	86	USA (NY)	<2 y	C-C	BL/Whz	212	First PD BL/wheeze	Paediatric OP lists (no wheeze)
17	88	China	<18 m	Cohort	Br/Pn	2227	PD Br/Pn	Population-based birth cohort
18	89	Samoa	<1 y	C-C	BL	80	RSV epidemic LRI	Well-child clinics
19	91	USA (AZ)	<1 y	Cohort	LRI	797	PD LRI	HMO-based cohort
20	92	Italy	<2 y	Survey	LRI	2797	Br/BL/Pn before 2 years	Population survey: age 7–11 years
21	92	Sweden	<12 m	Cohort	Br/Pn	192	Antibiotics for Br/Pn	Population-based birth cohort
22	96	USA (MN)	<2 y	Cohort	LRI	1424	LRI consultation	HMO-based cohort
23	96	S Africa	<2 y	Survey	LRI	726	PD RI before 2 years	Two schools survey: age 14–18 years
Community studies: wheezing illnesses								
15	85	N Zealand	<2 y	Cohort	Wheeze	1144	Wheeze/chesty cold	Population-based birth cohort
24	87	Denmark	<1 y	Cohort	Wheeze	5953	>1 episodes wheeze	Population-based birth cohort
17	88	China	<18 m	Cohort	Wheeze	2227	PD asthma	Population-based birth cohort
25	89	UK	<1 y	Trial	Wheeze	480	Wheeze by 1 year (reported)	Infants from allergic families
26	90	UK	<18 m	Trial	Wheeze	777	>3 wheeze or asthma	Infants <37 weeks gestation
27	91	Denmark	<18 m	Cohort	Wheeze	276	>2 episodes wheeze	Random sample of births
28	93	UK	<2 y	Cohort	Wheeze	1172	>3 episodes wheeze	Population-based birth cohort
29	93	USA (MA)	<12 m	Cohort	Wheeze	97	Wheeze or LRI adm.	Special lung function study
30	95	USA (AZ)	<3 y	Cohort	Wheeze	762	LRI with wheeze	HMO-based birth cohort
31	96	Australia	<1 y	Cohort	Wheeze	525	Bronchodilator therapy	Infants <33 weeks gestation
Community studies: upper and lower respiratory illnesses								
45	87	UK	<12 m	Cohort	U/LRI	1542	HV record of U/LRI	Population-based birth cohort
46	90	Australia	1–3 y	C-C	U/LRI	489	High U/LRI "score"	Population survey: low score
Hospital admission for lower respiratory illness								
1	74	Israel	<1 y	Cohort	Br/Pn (IP)	10672	Adm. for Br/Pn	Population-based birth cohort
32	78	UK	[b]	C-C	BL(IP)	70	RSV +ve BL adm.	Schoolmates at age 8 years
33	82	UK	<1 y	C-C	Br/Pn (IP)	400	Adm. for LRI	Classmates at age 7 years
34	83	USA (IA)	<2 y	Survey	LRI (IP)	1139	LRI adm. before 2 years	Population survey: age 6–12 years
35	84	USA (NY)	<2 y	C-C	BL (IP)	87	RSV+ adm. with LRI	Acute non-respiratory admission
36	87	UK	<5 y	Cohort	LRI (IP)	12727	Adm. for LRI	Population-based birth cohort
37	88	USA (GA)	<2 y	C-C	Pn/BL (IP)	301	Adm. for Pn/BL	Outpatient clinics
38	89	Canada	<2 y	Survey	LRI (IP)	4099	LRI adm. before 2 years	Population survey: age 7–12 years
39	92	Australia	5–15 m	C-C	BL (IP)	96	Bronchiolitis adm.	Non-respiratory admissions
40	93	China	<18 m	Cohort	Br/Pn (IP)	1007	Admitted for Br/Pn	Population-based birth cohort
41	94	Brazil	<2 y	C-C	Pn (IP)	1020	Pneumonia (*x* ray)	Neighbours
42	95	Sweden	4–18 m	C-C	Whz (IP)	308	Wheezy & breathless	Population sample, same area
Hospital admission for upper or lower respiratory illness								
47	78	Finland	<5 y	Cohort	U/LRI (IP)	3644	Adm. for U/LRI	Smoking & non-smoking mothers
48	85	UK	<12 m	Cohort	U/LRI (IP)	1542	Adm. for U/LRI	Population-based birth cohort
49	94	China	<18 m	Cohort	U/LRI (IP)	3285	Any respiratory adm.	Two population birth cohorts

OP/IP = out/inpatients; PD = physician diagnosed; C-C = case-control study; BL = acute bronchiolitis; Br = acute bronchitis; Pn = pneumonia; U/LRI = upper/lower respiratory illness; RSV = respiratory syncytial virus; Adm. = admission.
[a]Six Cities.
[b]"Infants".

specifically on illnesses associated with wheezing. Two publications[15 17] contributed independent data on both bronchitis/pneumonia and wheezing illnesses.

The results of these studies are summarised in table 2 and figs 1–3. All found an increased risk associated with parental smoking, including by the father only where this was assessed. Table 3 presents the results of meta-analyses, pooling the results of studies of early wheezing separately from those of unspecified lower respiratory illness, bronchitis, bronchiolitis or pneumonia. Although the effect of either parent smoking is similar for these two outcomes, maternal smoking appears to be relatively more important, and paternal smoking perhaps less important in studies which have ascertained wheezing illness specifically.

STUDIES OF HOSPITAL ADMISSIONS FOR LOWER RESPIRATORY ILLNESS

Twelve publications[1 32–42] were identified relating to hospital admissions for lower respiratory complaints in early life. Three did not differentiate between different forms of chest illness,[34 36 38] four related to bronchitis and/or pneumonia,[1 33 40 41] and five focused on admission for wheezing illness[42] or for bronchiolitis with[32 35] or without[37 39] confirmation of respiratory syncytial virus infection.

One cohort study included here[36] presented detailed findings only in relation to hospital admissions up to five years of age, but tabulations by age at admission suggest a similar strength of association between maternal smoking and admission for bronchitis or pneumonia at all ages from birth to five years. The results for all ages are therefore included in the meta-analyses.

The results of these studies are summarised in table 2 and figs 1–3. All except one study[41] found an increased risk associated with parental smoking. The results of meta-analyses are summarised in table 3. The pooled odds ratios are similar in magnitude to those derived from community studies.

Two case-control studies from South Africa[43] and the United Kingdom[44] were excluded from the quantitative overview because they present results only for a smoky atmosphere in the home. In the South African study the principal source of exposure was wood smoke. In the British study[44] infants admitted with suspected bronchiolitis were almost three times more likely to have a smoky atmosphere recorded by health visitors on a visit to the home at one

Table 2 Unadjusted relative risks (odds ratios) associated with parental smoking

				Odds ratios (95% CI) for smoking by:				*Dose-response present?*
Reference	*Outcome*	*Cases*	*Controls*	*Either parent*	*Mother*	*Father or other*[a]	*Both parents*	
Community studies: lower respiratory illnesses								
11	Br/Pn	239	1835	1.96 (1.38 to 2.80)	—	—	2.79 (1.87 to 4.15)	Yes (no. of smokers)
12	LRI	31	[b]	1.25 (0.81 to 1.93)				—
13	LRI	221	[b]	1.27 (1.11 to 1.46)				—
14	LRI	820	7708	1.85 (1.56 to 2.20)	1.69 (1.47 to 1.96)	1.51 (1.22 to 1.86)	1.36 (1.11 to 1.66)	Yes (cigs/day by mother)
15	Br/Pn	204	940	1.56 (1.15 to 2.12)	1.83 (1.35 to 2.49)	1.04 (0.65 to 1.65)	1.83 (1.22 to 2.74)	Yes (cigs/day by mother)
16	BL	53	159	3.21 (1.42 to 7.25)	2.33 (1.19 to 4.57)	—	—	—
17	Br/Pn	925	1302	1.25 (1.03 to 1.52)	[none smoke]	1.25 (1.03 to 1.52)	—	Yes (cigs/day in home)
18	BL	20	60	3.86 (0.81 to 18.4)				—
19	LRI	256	541	—	1.52 (1.07 to 2.15)#			Yes (cigs/day by mother)
20	LRI	473	2324	1.32 (1.05 to 1.65)	1.21 (0.99 to 1.48)	1.25 (0.97 to 1.62)	1.34 (1.02 to 1.75)	—
21	Br/Pn	20	172	3.25 (1.27 to 8.34)				—
22	LRI	1107	[b]	—	1.50 (1.20 to 1.80)#			—
23	LRI	100	626	1.75 (1.07 to 2.87)	2.18 (1.25 to 3.78)			—
Community studies: wheezing illnesses								
15	Wheeze	733	411	1.32 (1.04 to 1.69)	1.43 (1.10 to 1.86)	1.09 (0.77 to 1.53)	1.50 (1.05 to 2.12)	No (cigs/day by mother)
24	Wheeze	120	5833	—	2.85 (1.93 to 4.19)			No (cigs/day by mother)
17	Wheeze	78	2149	1.27 (0.71 to 2.28)	[none smoke]	1.27 (0.71 to 2.28)	—	—
25	Wheeze	166	314	2.04 (1.39 to 3.01)	2.25 (1.52 to 3.33)	1.38 (0.81 to 2.37)	—	—
26	Wheeze	175	602	1.70 (1.19 to 2.42)				—
27	Wheeze	59	217	1.88 (0.97 to 3.63)				—
28	Wheeze	127	1045	—	2.24 (1.51 to 3.32)			—
29	Wheeze	59	38	—	3.16 (1.24 to 8.04)			—
30	Wheeze	247	515	—	2.07 (1.34 to 3.19)			—
31	Wheeze	76	449	—	1.98 (1.21 to 3.23)			Yes (cigs/day by mother)
Community studies: upper and lower respiratory illnesses								
45	U/LRI	486	1056	1.68 (1.33 to 2.11)	1.52 (1.22 to 1.89)	1.50 (1.12 to 2.01)	1.74 (1.33 to 2.27)	No (no. of smokers)
46	U/LRI	200	200	—	2.43 (1.63 to 3.61)#			—
Hospital admission for lower respiratory illness								
1	Br/Pn	1049	9623	—	1.43 (1.18 to 1.75)			Yes (cigs/day by mother)
32	BL	35	35	—	2.65 (0.99 to 7.11)			—
33	Br/Pn	200	200	—	1.26 (0.83 to 1.92)			—
34	LRI	53	1086	2.09 (1.12 to 3.89)	1.32 (0.74 to 2.32)	2.30 (1.13 to 4.70)	1.59 (0.74 to 3.44)	Inverse to no. of smokers
35	BL	29	58	4.78 (1.76 to 13.0)				—
36	LRI	434	12293	1.46 (1.19 to 1.79)	1.63 (1.34 to 1.97)	1.05 (0.78 to 1.41)	1.69 (1.33 to 2.14)	Yes (cigs/day by mother)
37	BL	102	199	1.99 (?, p<0.05)#[c]				—
38	LRI	?	?	—	1.85 (1.53 to 2.23)#			—
39	BL	39	57	2.15 (0.76 to 6.10)	2.66 (1.15 to 6.15)	1.27 (0.38 to 4.22)	3.29 (1.77 to 6.14)	Yes (urinary cotinine)
40	Br/Pn	164	843	1.78 (1.18 to 2.68)	[none smoke]	1.78 (1.18 to 2.68)	—	Yes (cigs/day in home)
41	Pn	510	510	0.94 (0.72 to 1.22)	1.02 (0.79 to 1.30)	0.89 (0.64 to 1.24)	0.94 (0.69 to 1.29)	No (cigs/day in home)
42	Whz	112	196	2.17 (1.38 to 3.59)	2.04 (1.26 to 3.28)	1.77 (0.85 to 3.66)	2.23 (1.23 to 4.05)	Yes (urinary cotinine)
Hospital admission for upper or lower respiratory illness								
47	U/LRI	490	3154	—	1.89 (1.55 to 2.30)			—
48	U/LRI	41	1501	1.94 (0.94 to 3.99)	2.68 (1.41 to 5.10)	0.87 (0.29 to 2.56)	2.76 (1.28 to 5.96)	Yes (no. of smokers)
49	U/LRI	239	3046	1.49 (1.05 to 2.10)	[none smoke]	1.49 (1.05 to 2.10)	—	No (cigs/day in home)

Abbreviations as for table 1.
[a] In households where the mother did not smoke (compared with neither parent smoking).
[b] Results published as person-time incidence rates. Rate ratios, rather than odds ratios are shown.
[c] 95% confidence interval estimated as 1.00 to 3.96 for purposes of meta-analysis.
Odds ratio or relative risk cited in the paper without tabulated numerical data (elsewhere, odds ratios were calculated from tabulated numbers or percentages).

month of age (odds ratio 2.93, 95% CI 1.95 to 4.41).

STUDIES OF UPPER AND LOWER RESPIRATORY ILLNESS COMBINED

Five studies[45–49] presented data relating parental smoking to all respiratory illness without distinguishing between upper and lower respiratory diagnoses (table 1). Two of these[45 46] were based in the community, and three relate to hospital admissions for respiratory illness.[47–49] One of the latter studies[49] synthesised the results of three previous papers.[50–52]

The findings of these studies, summarised in table 2, are broadly in line with those studies which have concentrated on lower respiratory illnesses, and their inclusion in the overall meta-analysis changes the estimates of effect only slightly (table 3).

INDEPENDENCE OF CONFOUNDING

About half of the cohort studies, but only a quarter of the case-control or cross sectional studies, presented estimates of the effects of parental smoking, both before and after adjustment for potential confounding variables. Although a different range of confounding variables was controlled in each study, the effects of parental smoking are little altered by adjustment for measured confounders (table 4).

DOSE-RESPONSE RELATIONSHIPS

Nine of the 12 cohort studies which present evidence relating to dose-response within smoking families found a statistically significant relationship, either to the number of smokers or to the amount smoked in the household, or specifically by the mother (table 2). A formal meta-analysis of the dose-response relationship

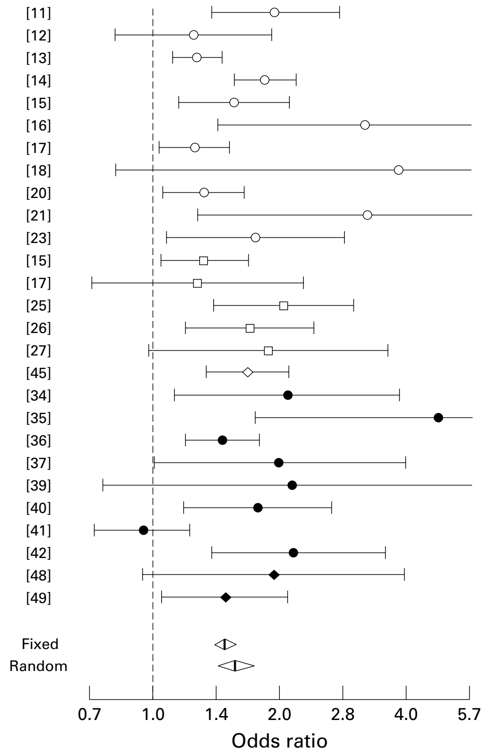

Figure 1 Odds ratios and 95% confidence intervals for effect of either parent smoking compared with neither smoking. The pooled odds ratios derived by fixed effects and random effects methods appear at the foot of the figure. The horizontal scale is logarithmic (base 2). Individual studies are denoted thus: circles = studies of lower respiratory illnesses; squares = studies of wheezing illnesses; diamonds = studies of upper and lower respiratory illnesses; open symbols = community studies; filled symbols = studies of hospitalised illnesses.

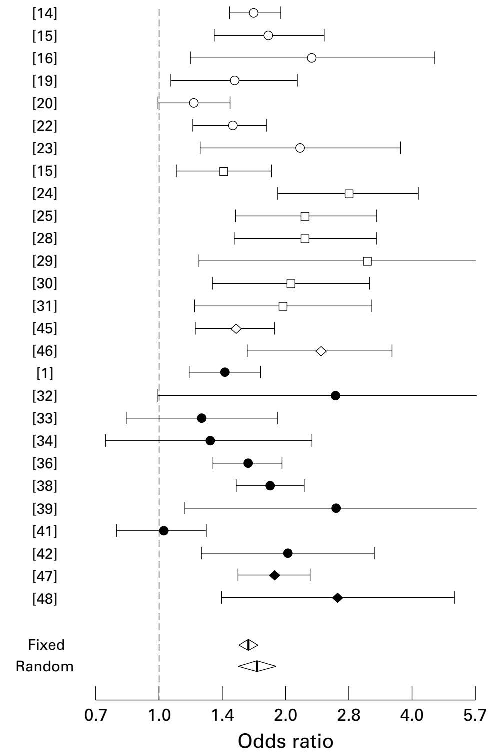

Figure 2 Odds ratios and 95% confidence intervals for effect of mother smoking compared with father only or neither parent smoking. Definitions of symbols as for fig 1.

is not possible. In contrast, the risk associated with both parents smoking was not substantially greater than that for either parent smoking. A comparison of both parents smoking with neither smoking was available for 11 studies[11 14 15 20 34 36 39 41 42 45 48] and the pooled odds ratio was 1.69 (95% CI 1.37 to 2.08)

In two case-control studies[39 42] urinary cotinine levels were measured as an objective marker of tobacco smoke exposure, and in both the levels were significantly higher in the case group. These results are consistent with another small case-control study of emergency room attendances for wheezing illness[53] which measured urinary cotinine levels but did not report in detail on parental smoking habits. None of these studies restricted their analysis to smoking families, and therefore the differences in cotinine levels may simply reflect the presence of smokers in the household, rather than evidence of a graded relationship to the amount of exposure to environmental tobacco smoke.

EFFECT ON SPECIFIC RESPIRATORY DIAGNOSES

Few papers have compared the effect of parental smoking on different specific clinical diagnoses, and the results are inconsistent with effects confined to tracheitis and bronchitis in one[13] but to wheezing and pneumonia (and not bronchitis or bronchiolitis) in another.[22] One cohort study explicitly distinguished between lower respiratory illnesses which were associated with wheezing and those which were not.[19] The proportion of cases exposed to maternal smoking (>20 cigarettes/day) was 14% in each subgroup. This is not entirely consistent with the pooled odds ratios obtained from community studies which suggest a stronger effect of maternal smoking in studies specifically of wheezing than in those including a broader range of chest illnesses (table 3).

Seven case-control studies focused specifically on bronchiolitis or illnesses associated with evidence of respiratory syncytial virus infection.[16 18 32 35 37 39 44] These generated a somewhat stronger effect than other studies, but this may reflect positive publication bias which is discussed further below.

EFFECT OF PARENTAL SMOKING AT DIFFERENT AGES

The early report by Colley *et al*[2] suggested that the effect of parental smoking on the incidence of bronchitis and pneumonia was most marked in the first year of life (odds ratio 1.96, 95% CI 1.30 to 2.99), declining thereafter with increasing age of the child to an inverse relationship in the fifth year. Results from the Dunedin, New Zealand cohort showed a similar pattern, with a slightly greater effect in the first than the second year[54] and little evidence of association with consultation for bronchitis or pneumonia after two years of age.[15]

Table 3 Pooled odds ratios, 95% confidence intervals and heterogeneity tests from meta-analyses

		Either parent	*Mother*	*Father only*
All studies	Number of studies	27	27	16
	Heterogeneity χ^2	55.1 (p<0.001)	60.7 (p<0.001)	18.6 (p=0.232)
	Odds ratio (fixed)	1.49 (1.40 to 1.58)	1.64 (1.55 to 1.73)	1.29 (1.19 to 1.41)
	and 95% CI (random)	1.57 (1.42 to 1.74)	1.72 (1.55 to 1.91)	1.29 (1.16 to 1.44)
Excluding studies which include upper respiratory illness	Number of studies	24	23	13
	Heterogeneity χ^2	52.2 (p<0.001)	51.8 (p<0.001)	16.3 (p=0.117)
	Odds ratio (fixed)	1.46 (1.37 to 1.56)	1.61 (1.51 to 1.71)	1.27 (1.15 to 1.39)
	and 95% CI (random)	1.57 (1.40 to 1.77)	1.69 (1.50 to 1.89)	1.26 (1.11 to 1.43)
Community studies of LRI, bronchitis and/or pneumonia	Number of studies	11	7	4
	Heterogeneity χ^2	25.7 (p=0.002)	11.3 (p=0.040)	3.03 (p=0.387)
	Odds ratio (fixed)	1.46 (1.35 to 1.58)	1.56 (1.43 to 1.71)	1.31 (1.16 to 1.48)
	and 95% CI (random)	1.54 (1.31 to 1.80)	1.57 (1.33 to 1.86)	[inappropriate]#
Community studies of wheezing illness	Number of studies	5	7	3
	Heterogeneity χ^2	4.65 (p=0.325)	11.1 (p=0.049)	0.59 (p=0.744)
	Odds ratio (fixed)	1.54 (1.30 to 1.81)	1.98 (1.71 to 2.30)	1.19 (0.92 to 1.53)
	and 95% CI (random)	1.55 (1.16 to 2.08)	2.08 (1.59 to 2.71)	[inappropriate]#
Hospital admission for LRI, bronchitis, bronchiolitis or pneumonia	Number of studies	8	9	6
	Heterogeneity χ^2	22.2 (p=0.002)	22.3 (p=0.004)	11.8 (p=0.037)
	Odds ratio (fixed)	1.45 (1.27 to 1.66)	1.54 (1.40 to 1.69)	1.21 (1.01 to 1.44)
	and 95% CI (random)	1.71 (1.21 to 2.40)	1.53 (1.25 to 1.86)	1.32 (0.87 to 2.00)

Number of studies too small for reliable random effects modelling. No significant heterogeneity of effects.

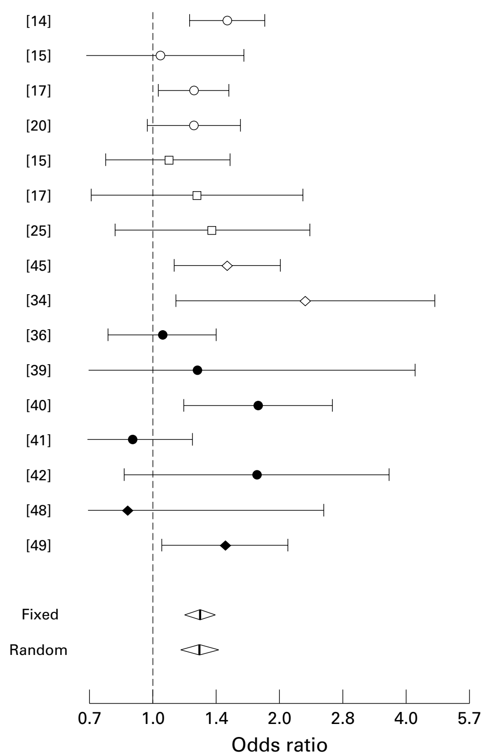

Figure 3 Odds ratios and 95% confidence intervals for effect of smoking by household members apart from the mother compared with neither parent smoking. Definition of symbols as for fig 1.

The effects of non-maternal smoking on admissions to hospital for respiratory disease in Shanghai were stronger before six months of age than in children aged 7–18 months.[17] However, a significantly increased risk persisted after six months of age for children exposed to more than 10 cigarettes per day in the home (incidence ratio 1.83, 95% CI 1.03 to 3.24). In the 1970 British cohort[36] the effect of maternal smoking on hospital admissions for wheezing illness, bronchitis, or pneumonia was similar at all ages up to five years.

EFFECT ON SUSCEPTIBLE SUBGROUPS

The effect of parental smoking on early respiratory illness has been reported in two controlled trials[25 26] and one cohort study[31] which recruited infants at high risk due to a parental history of allergy[25] or prematurity.[26 31] The odds ratios obtained from these studies were within the general range (table 2) and have therefore been included in the meta-analyses.

Only one study included here[49] permitted a direct comparison between high and low risk infants. In two Chinese cohorts an adverse effect of household smoking on hospital admissions for respiratory disease was evident among both low birthweight (<2.5 kg) babies (odds ratio 6.87, 95% CI 0.89 to 53.0) and normal birthweight infants (1.36, 95% CI 0.96 to 1.93). There was no statistically significant effect modification by birthweight (test for interaction, p=0.06).

PRENATAL VERSUS POSTNATAL EXPOSURE

The effects of smoking by other household members in homes where the mother did not smoke are summarised in tables 2 and 3. These are derived from three studies from China[17 40 49] which included no smoking mothers, and 11 from westernised countries where data were presented for smoking by the father only. The results are quantitatively consistent, and only two odds ratios are less than unity (fig 3). The pooled odds ratio obtained by meta-analysis is 1.29 (95% CI 1.16 to 1.44). In the Chinese studies this effect is independent of birthweight and a range of other confounding factors.[40 49]

Few studies have evaluated the effects of prenatal and postnatal maternal smoking in the same sample. In Western countries too few mothers change their smoking habits in the perinatal period to offer the statistical power to discriminate prenatal and postnatal effects reliably. For example, in the largest study based on a national British cohort[36] half of the children were born to mothers who smoked in pregnancy. Only 8% of mothers who smoked during pregnancy subsequently gave up, and

Table 4 Effect of adjustment for potential confounders

Reference	*Outcome*	*Exposure*	*Unadjusted odds ratio*	*Adjusted odds ratio*	*Factors adjusted for (matching variables in parentheses)*
Community studies: lower respiratory illnesses					
11	Br/Pn	Both v none	2.95	2.78	FH chest symptoms, sex, siblings, sibling illness
12	LRI				None
13	LRI				None
14	LRI				None
15	Br/Pn				[a]
16	BL	Mother smokes	2.33	2.68	(Age), SES, BF, siblings, crowding, FH asthma
17	Br/Pn	Others ≥10/day	1.33	1.31	Sex, BW, daycare, education, cooking fuel
18	BL				(Age)
19	LRI	Mother ≥10/day	1.82	1.74	FH chest illness, season of birth, daycare, crowding
20	LRI	Either parent	1.32	1.3	Age, sex, area, SES, sibs, domestic crowding, heating
21	Br/Pn				None
22	LRI	Mother smokes	[b]	1.5	FH asthma, BF, birth order, daycare, housing
23	LRI				None
Community studies: wheezing illnesses					
15	Wheeze				[a]
24	Wheeze	Mother ≥20/day	2.85	2.7	Sex, SES
17	Wheeze				None
25	Wheeze				None
26	Wheeze				None
27	Wheeze	Any smoking	1.88	2.4	Sex, SES
28	Wheeze	Mother smokes	2.24	2.2	Sex, low BW, FH allergy, season of birth [c]
29	Wheeze				None
30	Wheeze	Mother smokes	2.07	2.25	Sex, ethnicity, past allergy, FH asthma
31	Wheeze	Mother smokes	1.98	1.77	Duration of BF
Community studies: upper and lower respiratory illnesses					
45	U/LRI	Both v none	1.74	1.54	Maternal age, heating fuel
46	U/LRI	Mother smokes	2.43	2.06	Sex, sibs, FH RD, daycare, SES, stress, BF
Hospital admission for lower respiratory illness					
1	Br/Pn				BW, SES (stratified tabulations)
32	BL				(Age, sex, SES)
33	Br/Pn				(Age, height, school)
34	LRI				Gas cooking (stratified tabulations)
35	BL				(Age, sex, race, season, form of health insurance)
36	LRI				None
37	Pn/BL				(Age, sex)
38	LRI				None
39	BL				None
40	Br/Pn	Other ≥20/day	2.0	2.4	Sex, BF, BW, education, maternal age, cooking fuel
41	Pn				(Age)
42	Wheeze	Both parents	2.23	2.0	(Age), FH asthma, BF duration
Hospital admission for upper or lower respiratory illness					
47	U/LRI				None
48	U/LRI				None
49	U/LRI	Any smoking	1.49	1.48	Low BW

FH = family history; SES = socioeconomic status; BF = breast feeding; BW = birthweight; RD = respiratory disease; other abbreviations see table 1.
[a] An analysis of incidence to one year of age ref. 64 shows smoking effects are independent of BF and housing.
[b] No unadjusted relative risk given.
[c] Additional adjustment for FH asthma, pets, SES in ref. 65 (incidence to one year of age).

6% prenatal non-smokers smoked after the child was born. The rate of hospital admissions for lower respiratory illness differed between these two groups, but not significantly so (5.9% versus 3.1%, odds ratio 1.94, 95% CI 0.96 to 3.94). The effect of postnatal smoking by mothers who did not smoke in pregnancy compared with never smoking mothers was also non-significant (odds ratio 1.36, 95% CI 0.73 to 2.54), although it is interesting to note that it was consistent with the pooled effect of father only smoking in this and other studies (table 3).

One controlled intervention study has monitored the incidence of acute lower respiratory illness after an intervention designed to modify postnatal exposure to tobacco smoke.[55] Among 581 infants followed to six months of age there was no difference in the incidence of episodes of cough, wheeze, or rattling in the chest among the intervention group (1.6 episodes per child-year) and the control group (1.5 episodes per child-year). However, the intervention was of uncertain effectiveness in reducing tobacco smoke exposure, as mean cotinine levels did not differ between the study groups despite a reduction in reported smoke exposure of infants in the intervention group.

Discussion

The direction of the association between parental smoking and lower respiratory illness is generally consistent across different study designs, methods of case ascertainment, and diagnostic groupings (table 2). Only one study from Brazil[41] found an inverse relation (with pneumonia), but another South American study from Chile[56] found a highly significant doubling in risk of pneumonia in the offspring of mothers who smoked. The latter could not be included in the meta-analysis as no confidence intervals could be derived.

Some variation between studies in the size of odds ratios would be anticipated as patterns of smoking differed between countries and over time. This is reflected in statistically significant heterogeneity in many of the pooled analyses (table 3). For this reason, the summary odds ratios derived under the fixed effects assumption should be interpreted with caution. The random effects method is more appropriate in these circumstances and suggests an odds ratio of about 1.6 as the typical effect of either parent smoking on the incidence of early chest illness, whether ascertained by parental questionnaire, primary care contacts, or hospital admissions.

The papers cited were selected by mention of keywords relevant to passive smoking and children in the title or abstract. When cross-checked against previous reviews of passive smoking in children[57–59] no major omissions were identified, whereas our systematic search included relevant references not cited elsewhere. There is a possibility that our selection was biased towards studies reporting a positive association, since it is more likely that statistically significant findings would be mentioned in the abstract. Three of the higher odds ratios were derived from small case-control studies in which passive smoking was not the focus of the original research[16 18 35] and where bibliographical bias may have operated. The slightly higher pooled odds ratios obtained by the random effects than by the fixed effect method (table 3) reflects greater weight assigned by the random effects approach to these small studies with relatively large odds ratios. On the other hand, inclusion of the large Chinese studies[17 40 49] in the meta-analysis of the effect of either parent smoking will have had a conservative effect due to the absence of maternal smoking in these communities.

The nature of the common lower respiratory tract illnesses of infancy remains a subject of uncertainty and debate.[60 61] Although many appear to be triggered by viral infections, there is evidence of premorbid susceptibility related to lung function abnormalities detectable from birth.[62] Many early wheezing episodes, including bronchiolitis, probably form part of this spectrum of viral illnesses, although others may be the first evidence of more persistent childhood asthma with associated atopic manifestations.[30 61] Respiratory viruses are isolated with equal frequency from infants in smoking and non-smoking households.[12] The effect of parental smoking on the incidence of wheezing and non-wheezing illnesses appears similar, suggesting a general increase in susceptibility to clinical illness on exposure to respiratory infections, rather than influences on mechanisms more specifically related to asthma. Two such characteristics – allergic sensitisation and bronchial hyperresponsiveness – will be considered in detail in future reviews in this series.

The pooled results from families where the mother does not smoke suggest that this effect of parental smoking is at least partly due to postnatal (environmental) exposure to tobacco smoke in the home. The somewhat stronger effect of smoking by the mother than by other household members may be related to a higher degree of postnatal exposure from the mother as principal care giver, although there is insufficient evidence to exclude a specific adverse effect of maternal smoking during pregnancy, perhaps through its effect on intrauterine lung development.[29]

The effect of parental smoking is largely independent of confounding variables where these have been measured, suggesting that residual confounding by other factors is unlikely to be important. Thus it seems to be the smoking, rather than the family in which people smoke, which is the influential factor. It is therefore reasonable to conclude, as have recent overviews,[57–59] that there is a causal relationship between parental smoking and acute lower respiratory illness, at least in the first two years of life.

Appendix

Algorithm for random effects meta-analysis and meta-regression using GLIM:[63]

```
$units 27         ! Set to number of studies included in
                  ! meta-analysis
$var OR LCL UCL $read OR LCL UCL
$cal LNOR=%log(OR):
$cal SE=(%log(UCL) – %log (LCL))/(2*1.96)
$cal TAU2=SE**2       ! Variance of each log odds
$cal W=1 $weight W
$yvar LNOR
$fit $display e$ ! Fits ordinary least squares estimate
                  ! giving equal weight to each study

$mac IN           ! Calculates initial value for between
                  ! study variance SIGSQ
$cal %S=%CU((%YV – %FV)**2 – TAU2)/%SL
$print 'INITIAL SIGSQ= ' %S
$endmac

$mac SIG          ! Carries out one iteration to recalculate
                  ! SIGSQ
$cal %R=%S
$cal %S=%CU(((%YV – %FV)**2)/(1+TAU2/
%R)**2)/%CU(1/(1+TAU2/%R))
$cal %E=(%S – %R) * 100/%S: %A=%A – 1
$endmac

$mac REFIT        ! Refits model with weights combining
                  ! SIGSQ and TAU2
$cal %G=%F
$cal W=1/(%S+TAU2) $scale 1 $fit
$display e
$print 'NEW CHI-SQUARE, D.F.' %X2 %DF
$endmac

$mac ITER         ! Calls SIG repeatedly to produce new
                  ! SIGSQ (20 calls usually sufficient
                  ! for convergence) and then refits
                  ! model by calling REFIT
$cal %A=20 $while %A SIG
$use REFIT $print 'n= ' %SL 'NEW SIGSQ= ' %S
$endmac

$use IN
$use ITER         ! Call repeatedly until convergence
                  ! (five calls usually sufficient).
```

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